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22 July 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH HUMAN PHOSPHODIESTERASE 11A (PDE11A)**

(57) Abstract: The invention provides a human PDE11A which is associated with the disorders of the peripheral and central nervous system (Alzheimer), cardiovascular diseases, cancer (thyroid tumor, lung tumor, colon tumor), liver disease (liver cirrhosis) and genito-urinary diseases. The invention also provides assays for the identification of compounds useful in the treatment or prevention of disorders of the peripheral and central nervous system, cardiovascular diseases, cancer, liver disease and genito-urinary diseases. The invention also features compounds which bind to and/or activate or inhibit the activity of PDE11A as well as pharmaceutical compositions comprising such compounds.



WO 2004/029617 A3

INTERNATIONAL SEARCH REPORT

International Application No

/EP 03/10376

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/574 C12Q1/44 G01N33/68 A61K39/395 A61K48/00
A61K38/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 416 991 B1 (LANFEAR JERRY ET AL) 9 July 2002 (2002-07-09) column 24, line 21 - column 25, line 44; claims 6,7; figures 5A,5B,7; example XV -----	1-26
X	EP 0 967 284 A (PFIZER LTD ;PFIZER (US)) 29 December 1999 (1999-12-29) paragraphs [0058] - [0066], [0352], [0364]; claims 10-22 ----- -/--	1-26

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

1 March 2004

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28. 04. 2004

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/10376

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YUASA KEIZO ET AL: "Identification of rat cyclic nucleotide phosphodiesterase 11A (PDE11A). Comparison of rat and human PDE11A splicing variants" EUROPEAN JOURNAL OF BIOCHEMISTRY, BERLIN, DE, vol. 268, no. 16, August 2001 (2001-08), pages 4440-4448, XP002196953 ISSN: 0014-2956 figure 5; table 2 -----	1-26
X	WO 01/66716 A (HARUOKA MOTOKO ;KAWABATA AYAKO (JP); MIYAJI HIROMASA (JP); NAKAMUR) 13 September 2001 (2001-09-13) abstract; figure 9 -----	1-26
A	PEREZ-TORRES S ET AL: "Cellular expression of cAMP phosphodiesterase PDE4A, PDE4B and PDE4D mRNAs in Alzheimer's disease brains" SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 27, no. 1, 2001, page 1134, XP002271232 31st Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 10-15, 2001 ISSN: 0190-5295 abstract -----	1-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/10376

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
claims 1-26 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: -

Present claims 19-21,24-26 relate to a pharmaceutical compositions, their production and their use defined by reference to a desirable characteristic or property, namely binding to or regulating the activity of a PDE11A polypeptide/polynucleotide. No true technical characterization is given.

The claims cover all pharmaceutical compositions, their production and their use having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT or disclosure within the meaning of Article 5 PCT for only a very limited amount of such pharmaceutical compositions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT).

An attempt is made to define the pharmaceutical compositions, their production and their use by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, search has been carried out for those parts of the claims which appear to be clear and supported, namely those parts relating to the examples (antisense oligonucleotide, antibody).

Present claims 1-26 relate also to an extremely large number of possible diseases. In fact, the terms used to identify the different diseases are so broad and vague that a lack of clarity (and/or consiseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or consice), namely the relationship between PDE11A and specific diseases/tissues, based on table 1.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of disorders of the peripheral and central nervous system (particularly as disclosed on pg 56 (lines 9-12), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

2. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of cardiovascular diseases (particularly as disclosed on pg 58 (lines 17-18), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

3. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of cancer (particularly as disclosed on pg 63 (lines 4-11), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

4. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of liver disease (particularly as disclosed on pg 60 (lines 6-7), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

5. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of genitological diseases (particularly as disclosed on pg 59 (lines 13), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

6. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents
useful in the treatment of urological diseases (particularly
as disclosed on pg 59 (line 13), in methods of diagnosis of
said diseases, pharmaceutical compositions containing
therapeutic agents for the treatment of said diseases, their
production and their use

INTERNATIONAL SEARCH REPORT

International Application No

/EP 03/10376

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			AU 2721700 A	24-07-2000
			CA 2357146 A1	13-07-2000
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			WO 0040733 A1	13-07-2000

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			WO 0166716 A1	13-09-2001
